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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/672,049	09/29/2000	Johannes Platzek	SCH-1722	2997

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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 05/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/672,049	PLATZEK ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *6-15,17-22,26-38 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,16,23-25,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 11, 2005 has been entered.

Claims 1-5, 16, 23-25, 39, and 40 are examined to the extend they read on the elected invention.

Claims 6-15, 17-22, 26-38, and 41 are withdrawn from further consideration on merits as they are directed to non-elected invention and species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 16, 23-25, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Platzek et al. (WO 97/26017) in view of Milius et al. (Jew J. Chem 1992) or in view of Riess et al. (WO 93/01798, equivalent to EP 548096) is MAINTAINED for essentially the same reasons set forth in the Office Action mailed June 16, 2004.

The instant invention is directed toward a galenical formulation comprising parnmagnetic perfluoroalkyl and diamagnetic perfluoroalkyl compounds.

Platzek et al. teach perfluoroalkyl-substituted, paramagnetic metal complexes for use in NMR, X-ray diagnostics, radiodiagnostics, and radiotherapeutic agents. Specifically disclosed is Complex 1, Rf-L-M, wherein Rf is C8F17, L is a direct bond, and M is that of general formula X1 of the instant invention when Z1=Gd, q=1, p=0. The reference lacks diamagnetic perfluoroalkyl-containing substances. See pg. 2-pg. 3., pg. 162-180.

Milius et al. teaches perfluoroalkylated anionic sugar phosphodiesters that are utilized in numberous biomedical applications, such as in vivo oxygen carriers, contrast agents, and drug delivery systems, as surfactants or co-surfactants. Disclosed are compounds of formula Rf-L1-B2, wherein Rf is C8F17, L1 is CH2CH2, and B2 is a disaccharide. The use of these compounds in fluorocarbon emulsion impart improved control over the characteristics of injectable fluorocarbon emulsions, including particle

sizes and size distributions, viscosity, long term storage stability, intravascular persistence, aggregability, rate of and response to phagocytosis, and biodistribution. See entire disclosure.

Reiss et al. teaches compounds of formula (XVI) – Rf-L1-B2 of the instant invention, herein Rf is a fluorinated radical of 2-18 carbon atoms, L1 is a straight chain carbon chain with up to 20 carbon atoms that contains –S-, and wherein B2 is a polyhydroxyalkyl chain with at least two hydroxyl groups, see pg. 8, lines 10-56, which depict formula (I). These compounds can be used in preparations intended o facilitate diagnosis, in particular by radiography, sonography, or NMR, and thus can be used as contrast agents or markers, see pg. 17, last paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the periuoroalkyl-substituted, parâmaghetic metal complexes of Platzek et al. and the perfuoroalkyl anionic sugars of Milius et al. because of the expectation of achieving an intravenous fluorocarbon emulsion for imaging, with optimum particle sizes and size distributions, viscosity, long term storage stability, intravascular persistence, aggregability, rate of and response to phagocytosis, and biodistribution.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the periuoroalkyl-substituted, paramagnetic metal complexes of Platzek et al. and the compounds of Reiss et al. because of the expectation of achieving enhanced contrast images and because it is obvious to combine two compositions taught by the prior art to be useful for the same purpose to

form a third composition that is to be used for the very same pupose. *In re Kerkoven*, 205 USPQ 1069 (CCPA 1980).

Regarding the ratios and percent weights, it is respectfully pointed out that it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Response to Arguments

Applicant's arguments filed January 11, 2005 and the declaration by Dr. Misselwitz filed November 19, 2004 averring the presence of unexpected benefits have been fully considered but they are not persuasive. Examiner notes that it is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the unexpected benefits shown in the examples do not compare to the same agents disclosed in the closest prior arts. Lilius teaches synergistic effect of stability and particle size as a results of combining the perfluoroalkyl compounds therein and egg yolk phospholipids together. The examples in Dr. Misselwitz's declaration fails to compare the combination of the instant invention

and that of the cited prior arts. Furthermore, even if the unexpected benefits are indeed present, the results are not commensurate with the scope of the herein claimed subject matter. Examiner notes that the instant claims are very broad that basically encompass any and every combination of perfluoroalkyl compounds. And yet, the examples demonstrated in Dr. Misselwitz's declaration merely covers a few perfluoroalkyl compounds combinations. Therefore, it is seen that the instant claims are properly rejected under 35 USC 103(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617